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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,995	10/30/2003	Atul Navinchandra Parikh	309J-000740US	8835

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EXAMINER	
PADGETT, MARIANNE L	
ART UNIT	**PAPER NUMBER**
1762	

DATE MAILED: 05/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,995	PARIKH ET AL.	
	Examiner	Art Unit	
	Marianne L. Padgett	1762	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/4/04 & 3/15/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-140* is/are pending in the application.

4a) Of the above claim(s) *1-18,41 and 64-140* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/4/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant's election without traverse of Group II, method claims 19-40 and 42-63 in the reply filed on 3/15/05 is acknowledged.

2. Claims 22 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The examiner, who is a physical chemist, is unfamiliar with the terms "tethered lipid bilayer", "polymer-cushioned lipid bilayer", "...in a proteo-lipidic mixture", or "a hybrid lipid bilayer...and an inner self-assembly monolayer", and found no clear explanation thereof in the specification. The terms were found mentioned, but not defined on p. 2, 4, 15 and 34-35, while pages 27-29 and 85 discussed supported bilayer lipid membranes, but not the above terms and phrases. If definitions or explanations are some where in the 100-page specification, the examiner cannot find them.

For "tethered...", tethered how or to what or in what way does it define some structure? What does "polymer cushioned" necessitate? Is it part of, inside, outside in relation to the lipid bilayer? Assuming "proteo-" means protein, how are the proteins "in a ...mixture" that is a lipid bilayer? What range of structures or whatever does this encompass? Is it some specific configuration or just generically any mixture of protein with a lipid bilayer?

According to the examiner's organic chemistry text, a lipid bilayer is two layers of lipids with the polar ends exposed and the non-polar ends sandwiched between, so the structure of "a hybrid lipid bilayer comprising an outer lipid layer and an inner self assembled monolayer" is unclear or ambiguous, plus not explained by the specification. Is the monolayer necessarily a different lipid layer, because other wise it can not be a lipid bilayer, or is the term contradictory of the requirement of the independent claim as the monolayer is not required to be made of lipids, so NOT really a lipid bilayer at all, but a monolayer of

lipid and a monolayer of something else entirely, which is unspecified? These meaning can not determined from the specification by this examiners, nor from her available textbooks,

3. Claims 19-40 and 42-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Note the uncertainty in meaning of claims 22 and 45 discussed above in section 2.

In claims 20 – 21 and 43-44, it is unclear whether the plurality of masks and plurality of secondary lipid bilayers are intended to be all used in the same steps (iv-vi) at the same time and on the same primary lipid bilayer, or if they are successively applied or applied to different primary lipid bilayer, or some variation on these possibility, such that the scope of these steps is unclear or ambiguous.

In claims 30 and 53, it is unclear in what way the UV source is intended to be "adjustable". It is the wavelength or the intensity or the position or what?

In parts (iv) of claims 19 and 42, the phrases "non-lipid area corresponding to...UV –transparent area in the UV mask" is of uncertain scope, because while the phrasing implies that the patterns for the two areas are the same, it does not actually state how the areas correspond or necessitate any specific relationship, hence whether the implied meaning is intended or something broader (negative, positive, random, etc...) can not be definitively determined.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 19, 22-23, 26-29, 32-33, 35-39, 42, 45-46, 49-52, 55-56 & 58-59 are rejected under 35 U.S.C. 102((a) or (b)) as being clearly anticipated by Morigaki et al. "Patterning solid-supported Lipid Bilayer Membranes by Lithographic Polymerization of Diacetylene Lipid" (2001).

First it is noted that Morigaki et al (cited in applicants IDS) only has the year it was published, 2001, not the month, hence the examiner can not determine if it is an (a) or a (b) reference, since (1) the oldest 2 of the priority documents 60/422,902 (10/30/02) and 60/423,327 (10/31/02) are not IFW image (scanned), so not be checked for support of claims to those potential effective filing dates; and (2) can not ascertain if the article was published before or after 10/(30 or 31)/2001; however since the received date (p.174) of the Morigaki et al article was June 15, 2000, publication was probably early in 2001, so the reference is possibly a 102(b).

In Morigaki et al, see the title, Figure 1 and scheme 1 on p. 172, described in the 2-4th paragraphs on p. 172 (last ¶ bridging to 173), noting use of mask in 1(B), removal of non-irradiated lipids in 1(c) and deposition of new lipid bilayers in 1(D), where scheme 1 shows use of 254 nm wavelength UV radiation. The p. 173, first full paragraph and experimental section on p. 174, 3rd grouping of information teaches that the lipid bilayers deposited in the patterned openings were supplied in the form of vesicles of

phosphatidylcholine doped with fluorescently labeled lipid, hence has a different "profile" (defined p.2 of applicant's specification) than the polymerized lipid bilayer. Fig 3 (p. 173) shows an array with a bar scale of 200 μm, so wells or openings formed therein appear to be about 200 μm on a side, which is inside claimed values for dimension ranges, even without "or less" attached to all ranges. The last 2 paragraphs on p. 173, which bride to p.174 describe further possible structure and uses (using a polymeric 'cushion' layer as a spacer, covalently attaching the polymerized layer to the support via chemically reactive "head group", use in membrane molding and biomedical applications, such as inclusion of proteins or creating address able arrays).

6. Claims 30-31, 34, 40, 53, 54, 57 and 60-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morigaki et al.

Morigaki et al do not teach that their UV light source is "adjustable", however virtually any light source is adjustable in some manner, if only in the position one places it with respect to the substrate being treated, and it is a standard technique to optimize ones intensity or radiation doses according to that needed to effect a particular polymerization reaction, hence it would have been obvious to one of ordinary skill in the polymerization art to use a UV source capable of being optimized, i.e., adjusted, for the reaction of interest, in order to effectively and efficiently produce the taught effects.

While Morigaki et al teach UV sources, exemplified by 254 nm radiation, they do not say what specific device produces their UV light, however low pressure Hg vapor lamps are old and well known as standard source for the exemplified wavelength, hence would have been obvious as a known source of the taught 254 nm radiation.

Morigaki et al do not specify any particular pattern or density or size or number for the patterns made by their process or on their masks, but they illustrate an example and do exemplify array patterns, noting the process's usefulness for addressable arrays, hence it would have been obvious to make and design such arrays or masks for arrays to have number and size of openings or areas to be useful for the

particular procedure for which the end product is desired, especially noting that for the suggestion of modeling [cell] membrane systems or monitoring activities of protein incorporated in membranes. Considering the exemplary size in Fig. 3, (200 μm bar-scale gives a probable array density of around 1600 area/cm^2, so the mask probably would have had similar densities), the high densities as claimed would have been an obvious option, and optimized to desired end use.

In Morigaki et al's exemplary pattern, the polymerized lipid bilayers form the contiguous pattern, while the non-lipid areas (before coating with a second lipid bilayer) are non-contiguous squares, however it would have been obvious to one of ordinary skill in the art, that the polymerizable lipid could have been irradiated in any design, contiguous or non-contiguous, depending on end use, such as monitoring procedures or if all deposits are desired to be permanent or what combinations of lipids are desired to be deposited, and which areas are polymerizable. If a permanent array is desired, where both the grid and the wells will be permanently adhered such as might be desired for a standard or as a control used in monitoring, then the pattern could have been deposited in either order, grid or wells first, i.e., contiguous or non-continuous. It is noted, that while Morigaki et al do not teach that the 2nd lipid bilayer may be polymerizable, neither do they exclude it and for the above discussed possibility of creating a permanently deposited combination of lipids, the teachings of stabilization via polymerization (p. 172) would have been motivation to use taught polymerizable lipid like the 1st bilayer also for the 2nd deposit.

It is also noted that the suggestion at the top of p. 174 of use in "creation of addressable arrays of modified lipid bilayer membranes for combinatorial chemistry" could be taken as a suggestion to have the "secondary material" undergo chemical reactions, but is not further explained in this article.

7. Claims 20-21, 43-44 and 61-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morigaki et al as applied to claims 19, 22-23, 26-40, 42, 45-46 & 49-63 above, and further in view of Cremer et al "Creating Spatially Addressed Arrays of Planar Supported Fluid Phospholipid Membranes" (1999).

Cremer et al "...Addressed Arrays..." was cited by Morigaki et al with respect to the suggested combinatorial chemistry on p. 174, thereof, hence its teachings would have been obvious for use in Morigaki et al as suggested. Cremer et al's use of arrays with deposits of multiple different lipid bilayer (liposome) compositions placed into different wells for testing, such as lipids modified with Biotin to be reactive with the protein streptavidin, which is later applied to the array to cause a claimed chemical protein-ligand reaction, thus explicitly supplying an alternative chemical reaction and another secondary substance than other alternative discussed above. See Fig., 1-2 and 2nd –4th paragraphs.

As noted in section 3 above, the meanings of claims 20-21 and 43-44 are not particularly clear, so they cannot be very precisely treated, however while Morigaki et al teach masking, they do not teach plural mask, however as they do teach do teach that a possible use of their patterned lipid bilayer is to repeatedly deposit new lipid bilayers thereon (col. 2, p. 173) after removing previous 'secondary' deposits, which is one way to read the clamed plural secondary lipids (materials), or alternately the teaching suggest use as in Cremer et al, who explicitly deposit substantially different lipid bilayer composition in different wells, either consecutively or parallel, thus various modes of application of plural lipid bilayers are taught or suggested, although there is no explicit use of multiple masks. It would have been obvious to one of ordinary skill to use whatever number of masks is required to produce a desired pattern or design of the desired dimensions. As for repeating all the steps (i-vi), it would have been obvious to one of ordinary skill that the process could have been done any number of times that is desired, especially if one is making a product for sale or if one may need to conduct various different or repeated tests for research or for monitoring.

8. Claims 24-25 and 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morigaki et al as applied to claims 19, 22-23, 26-40, 42-46, 49-63 above, and further in view of Ulman, "Micropatterning Fluid membranes" (1997).

Morigaki et al only provides examples of planer supported lipid bilayers, not non-planar as in these claims. Note that all things or objects that exist in the real world are 3-dimendtional, even this sheet of paper, so any lipid bilayer whether planar or not is 3D, as required by one option of claim 25 or 48, since it has a length, a width and a thickness.

The article by Ulman et al is also directed to micropatterning lipid bilayers, where arrays are of interest and the exemplary membranes are formed in planar configurations (p. 1121, 2nd column, 1st 2 paragraphs; Fig. 1 and 2), however under the application section, (p. 1122, 2nd col.), Ulman et al teach that any shape surface may be used for assembly, nothing that it is the surface properties (not the shape) that are important to the assembly of the lipid bilayer membrane, therefore it would have been obvious to one of ordinary skill in the art to employ any shape, planar or nonplanar, as suggested by Ulman et al in the analogue process of Morigaki et al, as ability to use various shape substrates provides flexibility in end use and application, and is not expected to materially or adversely effect the patterning or deposition processes.

9. Other art cited in the IDS that is of interest and cumulative to the above rejections, includes Salomé et al "characterization..." which on p. 392-393 discusses preparation of lipid bilayers, which are vesicles, spherical supported and planar supported. Groves et al ("Micropatterning...Supports" and "Substrate...Membrane") & Kung et al ("Printing...Membranes" and "Patterning...Bilayers") all provide further teachings on relevant uses of patterned grids of lipid bilayers, although employ different initial patterning procedures.

The excerpt from UV Curing: Science and Technology (ed. by Pappas) is supplied as supporting evidence for the above assertion of Hg-lamps being common sources of 254 nm light (see p. 105 & 109).

Also if interest is Tan (5,217,455) who discusses various removal processes used on skin (i.e. on cell's with membranes that comprise lipid bilayers), but the lasers discussed therein (col. 3 & 8), use visible or IR wavelengths; Arnold et al (5,310,648) or Charych et al (6,080,423) who employ UV to cause

polymerization reactions involving liposomes or lipid bilayers, but the later is a solution process and Arnold et al, while using UV to polymerize lipid bilayers in the presence of a template molecule (protein), cannot be considered a process for using masking and does not deposit a second material or lipid bilayer in a pattern as claimed.

Salamon et al (5,521,702) is of interest for using stabilized lipid bilayers for analytical techniques of interest, but does not pattern them or treat them with UV via claimed techniques. Blackburn et al (6,846,654 B1) is teachings a lipid bilayer biosensor (fig. 11 discussed on col. 23-24), where catalytic antibodies are anchored to the BLM, but also does not teach patterning as claimed by applicant, in the construction of this sensor.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to M L. Padgett whose telephone number is (571) 272-1425. The examiner can normally be reached on Monday-Friday from about 8:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Timothy Meeks can be reached at (571) 272-1423. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct:uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. L. Padgett/af
April 15, 2005
May 17, 2005

MARIANNE PADGETT
PRIMARY EXAMINER